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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,616	07/02/2001	Aprile L. Pilon	116142/00170	3118

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EXAMINER	
KAPUST, RACHEL B	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/898,616	PILON ET AL.	
	Examiner	Art Unit	
	Rachel B. Kapust	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-100* is/are pending in the application.

4a) Of the above claim(s) *1-34,56-73 and 79-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-55 and 74-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II (encompassing claims 35-55 and 74-78) is acknowledged. The traversal is on the ground(s) that (1) there is not a substantial burden on the Examiner because a search of Group II should reveal prior art for the remaining claims of Groups I and III-V; (2) the need to file divisional applications would shorten the patent term of the non-elected claims; and (3) the examiner would need to conduct a duplicate, redundant search for the non-elected claims.

Regarding Applicant's argument that there is not a substantial search burden on the Examiner, as stated in the office action of paper no. 12, the different groups of proteins and methods represent different inventions and require different, non-contiguous searches, as evidenced by their different classification. They require separate searches of separate databases. The search for methods of use is separate because it requires additional considerations as to the methodology itself. To consider all of these groups would constitute an undue burden because each requires considerations that are separate from each of the others.

As for Applicant's arguments that the non-elected claims would have a shortened patent term and that the examiner would need to conduct duplicate searches for the non-elected claims in any divisional applications, Applicant's remarks are noted. However, the only relevant argument regarding the restriction requirement is the one regarding the search burden.

The restriction requirement is still deemed proper and is therefore made FINAL. Claims 1-34, 56-73, and 79-100 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.42(b). Claims 35-55 and 74-78 are under consideration.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an

application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (*i.e.*, continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. While Applicants have noted that the current application is a continuation-in-part of U.S. Serial No. 08/864,357, filed May 28, 1997, the current status of the parent nonprovisional application should be included.

Specification

The disclosure is objected to because of the following informalities: On pages 21, 23, and 24, the phrase "Seq. ID. Nos." should be changed to "SEQ ID NO". See MPEP 2422 and 37 CFR 1.821. Appropriate correction is required.

On page 13, the description of Figure 5 does not contain an appropriate legend. The symbols "●" and "■" are used in Figure 5, but the description does not distinguish which one is the growth curve for the master seed and which one is the growth curve for the production seed.

The use of the trademarks SARTOBIND™ (p. 25), MICROFLUIDIZER™ (p. 52), ECL™ (p. 54), SEPHAROSE™ (p. 49), and EZLOGIC™ (p. 56) have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claims 53 and 54 are objected to because of the following informalities: Claim 53 refers to "step h" in claim 49. Claim 49 does not have a "step h". It appears that claim 53 should instead refer to "step e" of claim 49. Similarly, claim 54 refers to "step i" of claim 49, and claim

49 does not have a "step i". It appears that claim 54 should instead refer to "step f" of claim 49. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 52 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 52 recites the limitation "anion exchange column" in reference to claim 49. However, claim 49 does not refer to an anion exchange column. There is insufficient antecedent basis for this limitation in the claim.

Claims 43 and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 43 recites the limitation "Chelating Sepharose Fast Flow" resin column. SEPHAROSE™ is a trademark. Claim 46 recites the limitation "Sartobind Q TFF membrane". SARTOBIND™ is a trademark. It appears that Applicants intend to use the trademarks as a limitation to identify or describe a particular product, thus the claim scope is uncertain since the trademark cannot be used properly to identify any particular product. MPEP 2173.05(u).

Claims 36 and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 36 and 50 refer to a gene comprising SEQ ID NOS: 1-4. It is not clear whether the gene is meant to comprise SEQ ID NO: 1, 2, 3 ***or*** 4 or whether the gene is meant to comprise SEQ ID NOS: 1, 2, 3, ***and*** 4.

Claims 74-78 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims lack a correlation step describing how the results of the assay allow the determination of success for determining the purity of the rhUG.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Torkkeli *et al.* (1978, *Biochim Biophys Acta* 544(3): 578-592) in view of Andresson *et al.* (1994, *J. Biol. Chem.* 269(29): 19081-19087) and Mourot *et al.* (1989, *Separation Science and Technology* 24(5 & 6): 353-367). Claim 49 is drawn to a method of purifying recombinant human uteroglobin (rhUG)

comprising cell lysis, filtering the lysis through a membrane, loading the filtrate onto an exchange column, and recovering pure rhUG. Torkkeli *et al.* teach a method of purifying a rabbit uteroglobin-like protein to apparent homogeneity. The method comprises successive chromatographies on hydroxyapatite, cation exchange, and anion exchange columns (p. 580-581). The method further comprises steps of concentrating the protein sample prior to each chromatographic step. However, Torkkeli *et al.* do not teach a method of purifying a rhUG.

Andersson *et al.* teach a method of purifying a rhUG (p. 19082). It would have been obvious to a person of ordinary skill in the art modify the method as taught by Torkkeli *et al.* by purifying a rhUG as opposed to a naturally occurring rabbit uteroglobin. It is a common technique in the art to engineer recombinant forms of proteins in order to increase the total yield of a purified protein (see for example Scopes, R.K. (1994) Protein Purification Principles and Practice, 3rd Edition (Cantor, C.R., ed) pp. 270-277, Springer-Verlag, New York). Moreover, Andersson *et al.* teach that rabbit uteroglobin is homologous to human uteroglobin, and they both bind certain steroids and metabolites of polychlorinated biphenyls (p. 19081). Therefore, it would have been obvious to a person of ordinary skill in the art to modify the method as taught by Torkkeli *et al.* by purifying a rhUG as opposed to a rabbit uteroglobin. Motivation to do so is provided by Andersson *et al.* who teach that (a) high level of protein expression can be achieved by expressing the rhUG in *E. coli* (p. 19085) and (b) rabbit uteroglobin and human uteroglobin are functionally similar (p. 19081). Moreover, a person of ordinary skill in the art would have expected that the modified purification method to work as well as the one exemplified. However, Torkkeli *et al.* and Andersson *et al.* do not teach using nominal molecular weight cut off (NMWCO) membranes when concentrating the protein samples.

Mourot *et al.* teach that the membrane separation process is often used in plasma products, protein processing, fermentation downstream processing, cell harvesting, protein desalting, and/or protein concentration (p. 353). NMWCOs are among the membranes commonly used (p. 354). Thus, it would have been obvious to a person of ordinary skill in the art to utilize nominal molecular weight cut off (NMWCO) membranes when concentrating the samples prior to chromatographic steps. Motivation to do so is provided by Torkkeli, in that it was desirable to concentrate the uteroglobin prior to chromatographic steps, and Mourot *et al.*

teach that NMWCOs are useful for concentrating proteins. A person of ordinary skill in the art would have expected the modified purification method to work as well as the one exemplified.

Claim 55 is rejected under 35 U.S.C. 103(a) as being unpatentable over Andersson *et al.* in view of U.S. Patent No. 4,691,009 and Shin *et al.* (1997, *Biotechnol. Prog.* 13: 249-257). Claim 55 is drawn to a method of producing a pharmaceutical grade rhUG by expressing the rhUG in a bacterial fermentation culture, inducing expression of the rhUG, and purifying the rhUG by using at least one filtration step and at least one exchange column. As state above, Andersson *et al.* teach a method of purifying a rhUG (p. 19082). Andersson *et al.* teach expression of rhUG in BL21(DE3) cells with induction by IPTG. Andersson *et al.* teach purification of rhUG by concentrating the rhUG fractions with an Amicon cell fitted with a YM-2 membrane (a NMWCO membrane) and then applying the rhUG to an anion exchange column. Andersson *et al.* further teach that the availability of large quantities of purified rhUG would be useful for structural and functional studies (p. 19086, column 2). However, Andersson *et al.* do not teach using fermenters for producing large quantities of rhUG.

Growing bacterial cells in fermenters is a very commonly used technique for producing large quantities of recombinant proteins. U.S. Patent No. 4,691,009 teaches the large-scale production of recombinant proteins in fermenters (column 1). Shin *et al.* teach that fermenation is a key bioprocess technology in terms of the production of recombinant proteins (p. 249). In order to produce a greater amount of purified protein, it would have been obvious to a person of ordinary skill in the art to scale-up the protein expression as taught by Andersson *et al.* by using a fermentation method as taught by Shin *et al.* or U.S. Patent No. 4,691,009. Motivation to do so is provided by Andersson *et al.* who teach that large quantities of purified recombinant uteroglobin are desirable. Moreover, a person of ordinary skill in the art would have expected the modified protein production method to work as well as the one exemplified.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 35-55 and 74-78 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 35-41, 48-61, and 80-84 of copending Application No. 10/187498. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

NO CLAIMS ARE ALLOWED.

The following articles, patents, and published patent applications were found by the Examiner during the art search, and while not relied upon are considered pertinent to the instant application:

Mantile *et al.* (1993), J. Biol. Chem. 268(27): 20343-20351

Miele *et al.* (1990), J. Biol. Chem. 265(11): 6427-6435

Peter *et al.* (1989), Protein Eng. 3(1): 61-66

U.S. Patent No. 5,266,562 (Mukherjee *et al.*)

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel B. Kapust whose telephone number is (703) 305-0634. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm. Please note for your records that as of January 20, 2004 the examiner's new telephone number will be (571) 272-0886.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RBK
1/20/04